Weddington
10/766118

FILE 'REGISTRY' ENTERED AT 09:20:39 ON 18 FEB 2005
E PHYTANIC ACID
E PHYTANIC ACID/CN 5
L1 1 SEA ABB=ON PLU=ON "PHYTANIC ACID"/CN

FILE 'CAPLUS' ENTERED AT 09:21:16 ON 18 FEB 2005
L2 585 SEA ABB=ON PLU=ON L1 OR PHYTANIC
L3 19967 SEA ABB=ON PLU=ON NIDDM OR ("NON" INSULIN OR NONINSULIN)(W)DE PEND? OR DIABETES(5A)(TYPE(W)(II OR 2) OR ADULT(W)(ONSET OR ON SET) OR STABLE) OR MODY
L4 7 SEA ABB=ON PLU=ON L2 AND L3
L5 12 SEA ABB=ON PLU=ON L2 AND DIABET?

L6 12 SEA ABB=ON PLU=ON L4 OR L5

L6 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 20 Dec 2004
ACCESSION NUMBER: 2004:1088101 CAPLUS
TITLE: Up-regulation of PPARγ coactivator-1α as a strategy for preventing and reversing insulin resistance and obesity
AUTHOR(S): McCarty, Mark F.
CORPORATE SOURCE: NutriGuard Research, 1051 Hermes Ave., Encinitas, CA, 92024, USA
SOURCE: Medical Hypotheses (2005), 64(2), 399-407
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Excessive accumulation of triglycerides and certain fatty acid derivs. in skeletal muscle and other tissues appears to mediate many of the adverse effects of insulin resistance syndrome. Although fatty diets and obesity can promote such accumulation, deficient capacity for fatty acid oxidation can also contribute in this regard. Indeed, in subjects who are insulin resistant, **diabetic**, and/or obese, fatty acid oxidation by skeletal muscle tends to be inefficient, reflecting decreased expression of mitochondria and mitochondrial enzymes in muscle. This phenomenon is not corrected by weight loss, is not simply reflective of subnormal phys. activity, and is also seen in lean first-degree relatives of **diabetics**; thus, it appears to be primarily attributable to genetic factors. Recent studies indicate that decreased expression of PPARγ coactivator-1α (PGC-1α), a "master switch" which induces mitochondrial biogenesis by supporting the transcriptional activity of the nuclear respiratory factors, may largely account for the diminished oxidative capacity of subjects prone to insulin resistance. Thus, feasible measures which up-regulate PGC-1α may be useful for preventing and treating insulin resistance and obesity. These may include exercise training, metformin and other agents which stimulate AMP-activated kinase, high-dose biotin, and PPARδ agonists. Drugs which are specific agonists for PPARδ show remarkable efficacy in rodent models of insulin resistance, **diabetes**, and obesity, and are currently being evaluated clin. **Phytanic** acid, a branched-chain fatty acid found in omnivore diets, can also activate PPARδ, and thus should be examined with respect to its impact on mitochondrial biogenesis and insulin sensitivity.

Searcher : Shears 571-272-2528

L6 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 10 Nov 2004
ACCESSION NUMBER: 2004:949902 CAPLUS
TITLE: Nutraceutical resources for **diabetes** prevention - an update
AUTHOR(S): McCarty, Mark F.
CORPORATE SOURCE: NutriGuard Research, Encinitas, CA, 92024, USA
SOURCE: Medical Hypotheses (2004), Volume Date 2005, 64(1), 151-158
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is considerable need for safe agents that can reduce risk for **diabetes** in at-risk subjects. Although certain drugs - including metformin, acarbose, and orlistat - have shown **diabetes** -preventive activity in large randomized studies, nutraceuticals have potential in this regard as well. Natural agents which slow carbohydrate absorption may mimic the protective effect of acarbose; these include: soluble fiber - most notably glucomannan; chlorogenic acid - likely responsible for reduction in **diabetes** risk associated with heavy coffee intake; and legume-derived α-amylase inhibitors. There does not appear to be a natural lipase inhibitor functionally equivalent to orlistat, although there are poorly documented claims for Cassia nomame exts. Metformin's efficacy reflects activation of AMP-activated kinase; there is preliminary evidence that certain compds. in barley malt have similar activity, without the side effects associated with metformin. In supraphysiol. concns., biotin directly activates soluble guanylate cyclase; this implies that, at some sufficient intake, biotin should exert effects on β cells, the liver, and skeletal muscle that favor good glucose tolerance and maintenance of effective β cell function. Good magnesium status is associated with reduced **diabetes** risk and superior insulin sensitivity in recent epidemiol.; ample intakes of chromium picolinate appear to promote insulin sensitivity in many individuals and improve glycemic control in some **diabetics**; calcium/vitamin D may help preserve insulin sensitivity by preventing secondary hyperparathyroidism. Although conjugated linoleic acid - like thiazolidinediones, a PPAR-γ agonist - has not aided insulin sensitivity in clin. trials, the natural rexinoid **phytanic** acid exerts thiazolidinedione-like effect in animals and cell cultures, and merits clin. examination Other natural agents with the potential to treat and possibly prevent **diabetes** include exts. of bitter melon and of cinnamon. Nutraceuticals featuring meaningful doses of combinations of these agents would likely have substantial **diabetes**-preventive efficacy, and presumably could be marketed legally as aids to good glucose tolerance and insulin sensitivity.
REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 May 2004
ACCESSION NUMBER: 2004:412796 CAPLUS
DOCUMENT NUMBER: 140:395555

TITLE: Antidiabetic nutraceutical compositions comprising epigallocatechin gallate
INVENTOR(S): Raederstorff, Daniel; Teixeira, Sandra Renata; Weber, Peter
PATENT ASSIGNEE(S): DSM Ip Assets B.V., Neth.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041257	A2	20040521	WO 2003-EP10838	20030930
WO 2004041257	A3	20040805		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-24804 A 20021107

AB The invention relates to nutraceutical compns. comprising at least two ingredients from the groups of epigallocatechin gallate, pantethine or a metabolite thereof, **phytanic** acid, lipoic acid, policosanol and coenzyme Q-10 and their use in the treatment or prevention of **diabetes** or obesity.

IT **14721-66-5, Phytanic** acid
RL: FFD (Food or feed use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic nutraceutical compns. comprising epigallocatechin gallate)

L6 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 06 May 2004
ACCESSION NUMBER: 2004:368900 CAPLUS
DOCUMENT NUMBER: 140:395235
TITLE: Nuclear hormone receptor compounds such as β-ionol and fatty acid analogs for the treatment of cancer and skin disorders.
INVENTOR(S): Delong, Mitchell Anthony; Biedermann, Kimberly Ann; Bissett, Donald Lynn; Boyer, Angelique Sun; Cohen, Scott Louis; Snider, Catherine Elizabeth
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037213	A2	20040506	WO 2003-US34155	20031023
WO 2004037213	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004131648	A1	20040708	US 2002-279397	20021024
PRIORITY APPLN. INFO.:			US 2002-279397 A	20021024
OTHER SOURCE(S):	MARPAT 140:395235			

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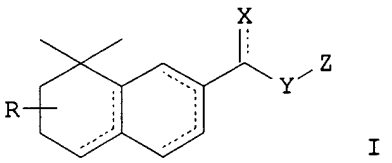

I

AB Title compds. e.g. [I; X = single or double bonded moiety comprising 0-12 (substituted) C atoms, 0-2 heteroatoms; Z = single, double, or triple bonded moiety comprising 0-12 C atoms in a chain, optionally including (substituted) cycloalkyl, aryl rings; Y = (CH2)n; n = 0-3; R = (substituted) alkyl, cycloalkyl, aryl], are claimed. (no synthetic data). Title compds. are believed to function as RXR, RAR and/or PPAR receptor ligands to encourage skin differentiation and discourage excess skin proliferation.

IT **14721-66-5, Phytanic** acid
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nuclear hormone receptor compds. such as β-ionol and fatty acid analogs for the treatment of cancer and skin disorders)

L6 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 26 Mar 2004

ACCESSION NUMBER:	2004:251322 CAPLUS
DOCUMENT NUMBER:	140:385310
TITLE:	Retinoids and retinoid receptors in the control of energy balance: novel pharmacological strategies in obesity and **diabetes**
AUTHOR(S):	Villarroya, F.; Iglesias, R.; Giralt, M.
CORPORATE SOURCE:	Department of Biochemistry and Molecular Biology, University of Barcelona, Barcelona, E-08028, Spain
SOURCE:	Current Medicinal Chemistry (2004), 11(6), 795-805 CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER:	Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Obesity and **type II diabetes** are closely related metabolic diseases with an increasing incidence worldwide. No clear-cut pharmacol. treatment for these complex metabolic disturbances is available despite current efforts. New directions and perspectives for the pharmacol. or nutritional treatment of these diseases should be defined. In recent years, a growing body of evidence shows that retinoids and retinoic acid receptors are involved in the control of biol. aspects (e.g. adiposity and energy expenditure mechanisms), which offers great potential for research on the treatment of obesity and **type II diabetes**. All-trans retinoic acid is known to inhibit adipocyte differentiation, whereas, mols. activating the retinoid X-receptor (rexinoids) promote the differentiation of adipocytes. Treatment with rexinoids ameliorates glycemic control in rodent models of **type II diabetes** and obesity, although other findings indicate similar pos. effects by inhibiting the receptor. Moreover, natural products of dietary origin, such as **phytanic** acid can activate RXR and thus, trigger adipose cell differentiation. Finally, the activation of retinoic acid receptors or retinoid X receptors has been reported to induce the gene expression of uncoupling proteins, which are mitochondrial proteins involved in the regulation of energy expenditure and fatty acid metabolism Further research is required to exploit the capacities of the retinoid-dependent pathways of regulation of adiposity, insulin sensitivity and energy expenditure for drug development in metabolic disturbances.
REFERENCE COUNT: 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 05 Mar 2004
ACCESSION NUMBER: 2004:182642 CAPLUS
DOCUMENT NUMBER: 140:216524
TITLE: Novel nutraceutical compositions comprising biotin
INVENTOR(S): Eggersdorfer, Manfred Ludwig; Raederstorff, Daniel; Teixeira, Sandra Renata; Weber, Peter
PATENT ASSIGNEE(S): DSM IP Assets B.V., Neth.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017766	A1	20040304	WO 2003-EP9112	20030818

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-18847 A 20020823
EP 2003-14625 A 20030626

AB Nutraceutical compns. comprise biotin in an amount sufficient to administer to a subject a daily dosage of 0.01 mg per kg body weight to about 3 mg per kg body weight and at least one addnl. component selected from pantethine or a metabolite thereof, EGCG, **phytanic** acid, lipoic acid and policosanol. The compns. are useful for the treatment of both type 1 and 2 **diabetes**, and for the prevention of **type 2 diabetes** in those individuals with pre-**diabetes**, or impaired glucose tolerance (IGT) or obesity.

IT **14721-66-5**, **Phytanic** acid
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nutraceutical compns. comprising biotin for treatment of **diabetes**, glucose tolerance and obesity)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 08 Nov 2002
ACCESSION NUMBER: 2002:849656 CAPLUS
DOCUMENT NUMBER: 137:338098
TITLE: Preparation of pharmaceutically active uridine ester nucleosides against a variety of diseases
INVENTOR(S): Susilo, Rudy
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088159	A1	20021107	WO 2002-EP4725	20020429
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EE 200300536	A	20040216	EE 2003-536	20020429
EP 1390378	A1	20040225	EP 2002-766645	20020429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009320	A	20040720	BR 2002-9320	20020429
JP 2004531543	T2	20041014	JP 2002-585457	20020429
NO 2003004782	A	20031212	NO 2003-4782	20031024

US 2004121979	A1	20040624	US 2003-476287		20031029
BG 108299	A	20040930	BG 2003-108299		20031029
PRIORITY APPLN. INFO.:			EP 2001-110608	A	20010430
			US 2001-288090P	P	20010503
			EP 2001-124879	A	20011018
			US 2001-330429P	P	20011022
			WO 2002-EP4725	W	20020429

OTHER SOURCE(S): MARPAT 137:338098
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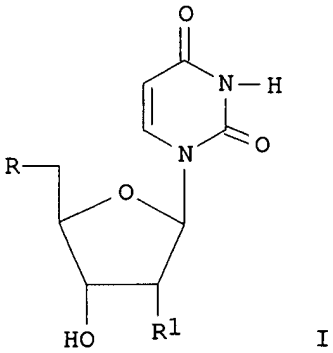

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AB The present invention relates to novel uridine esters I, wherein R represents a carboxylic acid residue, preferably a fatty acid residue and R1 represents hydrogen or a hydroxy group, their use as pharmaceutically active agents against a variety of diseases, methods for the preparation of said uridine esters and pharmaceutical compns. containing at least one uridine ester as active ingredient. The present invention relates also to a drug combination comprising free fatty acids and/or fatty acid esters and uridine, deoxyuridine, uridine monophosphate and/or deoxyuridine monophosphate, and to the use of such a drug combination. Thus, I [R = OCO(CH:CHCH2)6Et, R1 = OH] was prepared and tested in NMRI mice against a variety of diseases such as **diabetes**, polyneuropathy, and neuroprotective effects. Title compds were prepared as stimulant drug and/or for prophylaxis and/or treatment of **diabetes** mellitus Type I and **Type II**, inflammation, cancer, necrosis, gastric ulcers, neurodegenerative diseases (Alzheimer's disease, Parkinson's disease), neuropathic diseases, neuropathic pain and polyneuropathy, peripheral and/or central nerve diseases, degradation of the peripheral and/or central nerve system, heavy metal poisoning, ischemic diseases and ischemic heart disease, liver diseases and dysfunction of liver, allergies, cardiovascular diseases, Chlamydia pneumoniae, depression, obesity, stroke, pain, and/or retroviral infections (HIV, AIDS), including opportunistic infections. Dihomo-γ-linolenic acid Arachidonic acid 7,10,13,16-Docosatetraenoic acid α-Linolenic acid Stearidonic acid 8,11,14,17-Eicosatetraenoic acid γ-Linolenic acid.

IT **14721-66-5**, **Phytanic** acid
RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Aug 2002
ACCESSION NUMBER: 2002:624408 CAPLUS
DOCUMENT NUMBER: 138:348534
TITLE: The chlorophyll-derived metabolite **phytanic** acid induces white adipocyte differentiation
AUTHOR(S): Schlueter, A.; Yubero, P.; Iglesias, R.; Giralt, M.; Villarroya, F.
CORPORATE SOURCE: Department de Bioquimica i Biologia Molecular, Universitat de Barcelona, Barcelona, Spain
SOURCE: International Journal of Obesity (2002), 26(9), 1277-1280
CODEN: IJOBDP; ISSN: 0307-0565
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Phytanic** acid is a derivative of the phytol side-chain of chlorophyll. It appears in humans following the ingestion of fat-containing foods and is present in human blood at a low micromolar concentration It may activate retinoid X receptors (RXR) or peroxisome proliferator-activated receptor (PPAR) α in vitro. **Phytanic** acid induced the adipocyte differentiation of 3T3-L1 cells in culture as assessed by accumulation of lipid droplets and induction of the aP2 mRNA marker. This effect was mimicked by a synthetic activator of RXR but not by a PPARα agonist or by palmitic acid. In human pre-adipocytes in primary culture, **phytanic** acid also induced adipocyte differentiation. These findings indicate that **phytanic** acid may act as a natural rexinoid in adipose cells and suggest a potential use in the treatment of human **type 2 diabetes** and obesity.
IT **14721-66-5, Phytanic** acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorophyll-derived metabolite **phytanic** acid induces white adipocyte differentiation)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 09 May 2002
ACCESSION NUMBER: 2002:343937 CAPLUS
DOCUMENT NUMBER: 137:304593
TITLE: **Phytanic** acid, a natural peroxisome proliferator-activated receptor agonist, regulates glucose metabolism in rat primary hepatocytes
AUTHOR(S): Heim, Manuel; Johnson, James; Boess, Franziska; Bendik, Igor; Weber, Peter; Hunziker, Willi; Fluehmann, Beat
CORPORATE SOURCE: Research and Development, Department of Human Nutrition and Health, Roche Vitamins, Basel, 4070, Switz.
SOURCE: FASEB Journal (2002), 16(7), 718-720, 10.1096/fj.01-0816fje
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Phytanic** acid, a metabolite of chlorophyll, is part of the human diet and is present in normal human serum at low micromolar concns. It was previously shown to be a ligand of the 9-cis-retinoic acid receptor and peroxisome proliferator-activated receptor (PPAR) α. PPAR agonists are widely used in the treatment of **type 2 diabetes**. This work reports that **phytanic** acid is not only a transactivator of PPARα, but it also acts via PPARβ and PPARγ in CV-1 cells cotransfected with the resp. full-length receptor and an acyl-CoA oxidase-PPAR-responsive element-luciferase construct. In contrast to other fatty acids, **phytanic** acid at physiol. concns. enhanced the uptake of 2-deoxy-D-glucose in rat primary hepatocytes. This result could be explained by the increase in the expression of mRNAs for glucose transporters-1 and -2 and glucokinase, as determined by quant. real-time reverse transcriptase-polymerase chain reaction.
Compared with the PPARγ-specific agonist ciglitazone, **phytanic** acid exerted only minor effects on the differentiation of C3H1OT1/2 cells into mature adipocytes. These results demonstrate that **phytanic** acid acts via different PPAR isoforms to modulate expression of genes involved in glucose metabolism, thus suggesting a potential role of **phytanic** acid in the management of insulin resistance.
IT **14721-66-5, Phytanic** acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**phytanic** acid, a peroxisome proliferator-activated receptor agonist, regulation of glucose metabolism in hepatocytes)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 08 Feb 2002
ACCESSION NUMBER: 2002:104617 CAPLUS
DOCUMENT NUMBER: 136:145248
TITLE: Use of **phytanic** acid for the treatment of **diabetes** and other conditions associated with impaired glucose tolerance
INVENTOR(S): Fluehmann, Beat; Heim, Manuel; Hunziker, Willi; Weber, Peter
PATENT ASSIGNEE(S): Roche Vitamins A.-G., Switz.
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1177789	A2	20020206	EP 2001-118230	20010730
EP 1177789	A3	20030129		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO

US 2002082298	A1	20020627	US 2001-915152	20010725
US 6784207	B2	20040831		
JP 2002104964	A2	20020410	JP 2001-233070	20010801
CA 2353805	AA	20020204	CA 2001-2353805	20010803
BR 2001003209	A	20020326	BR 2001-3209	20010803
CN 1365667	A	20020828	CN 2001-124878	20010803
US 2004138181	A1	20040715	US 2004-766118	20040127
PRIORITY APPLN. INFO.:			EP 2000-116848	A 20000804
			US 2001-915152	A3 20010725

AB A method is provided for the treatment or prevention of preferably **non-insulin dependent** (**NIDDM** or so-called **Type II**) **diabetes** mellitus, or other conditions associated with impaired glucose tolerance, e.g. obesity, and in particular to the use of **phytanic** acid derivs. for the treatment or prevention.

IT **14721-66-5, Phytanic** acid **14721-66-5D, Phytanic** acid, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**phytanic** acid for the treatment of **diabetes** and other conditions associated with impaired glucose tolerance)

L6 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Mar 2001
ACCESSION NUMBER: 2001:219080 CAPLUS
DOCUMENT NUMBER: 135:175058
TITLE: The chlorophyll metabolite **phytanic** acid is a natural rexinoid - potential for treatment and prevention of **diabetes**
AUTHOR(S): McCarty, M. F.
CORPORATE SOURCE: Pantox Laboratories, San Diego, CA, 92109, USA
SOURCE: Medical Hypotheses (2001), 56(2), 217-219
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthetic ligands of the retinoid X receptor (RXR) have shown antidiabetic activity in mice, apparently owing to the fact that they stimulate the transcriptional activity of PPAR-γ/RXR heterodimers, much like thiazolidinedione drugs. The chlorophyll metabolite **phytanic** acid was shown to be a natural ligand for RXR, active in concns. near its physiol. levels. It is thus reasonable to suspect that **phytanic** acid may have utility for treatment and prevention of human **type 2 diabetes**. **Phytanic** acid may mimic or complement various effects of conjugated linoleic acids, which were shown to activate PPAR-γ/RXR and prevent rodent **diabetes**. Administration of hydrolyzed chlorophyll may represent the most cost-effective strategy for raising human tissue levels of **phytanic** acid.

IT **14721-66-5, Phytanic** acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**phytanic** acid for treatment and prevention of **diabetes**)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1972:473445 CAPLUS
DOCUMENT NUMBER: 77:73445
TITLE: Plasma free fatty acids and obesity
AUTHOR(S): Badinand, A.; Losman, M.
CORPORATE SOURCE: Lab. Cent. Chim. Biol., Hop. E. Herriot, Lyons, Fr.
SOURCE: Bollettino Chimico Farmaceutico (1972), 111(3), 147-58
CODEN: BCFAAI; ISSN: 0006-6648
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB Anal. of plasma free fatty acids and adipose tissue fatty acids of 8 human controls, 18 obese subjects, and 5 **diabetics** by thin-layer and gas chromatog. showed a higher concentration of stearic and palmitic acid in the plasma than in adipose tissue, particularly in obese subjects. In contrast, concentration of oleic acid is higher in adipose tissue. Its concentration is lowest in some obese subjects. The relatively high concentration of **phytanic** acid in plasma in comparison to adipose tissue indicate that its origin is not endogenous.
IT **14721-66-5**
RL: BIOL (Biological study)
(of blood plasma, in obesity, **diabetes** in relation to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 09:24:31 ON 18 FEB 2005)
L7 44 S L6
L8 30 DUP REM L7 (14 DUPLICATES REMOVED)

L8 ANSWER 1 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-066498 [07] WPIDS
DOC. NO. CPI: C2005-023331
TITLE: Achieving increased level of e.g. peroxisome proliferator-activated receptor heterodimer activator in livestock product e.g. milk, eggs involves ingesting livestock animal with product containing the activator.
DERWENT CLASS: D13
INVENTOR(S): DE KEYSER, L
PATENT ASSIGNEE(S): (IETI-N) IET INT ENG & TRADING
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005000036	A1	20050106	(200507)*	EN	47

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005000036	A1	WO 2004-EP51205	20040623

PRIORITY APPLN. INFO: WO 2003-BE112 20030626
AN 2005-066498 [07] WPIDS
AB WO2005000036 A UPAB: 20050128
NOVELTY - A non therapeutic method for achieving an increased level of at least one peroxisome proliferator-activated receptor (PPAR) or retinoid-X-receptor (RXR) heterodimer activator in a livestock product involves ingesting to livestock animals in agri- or aquaculture, at least one product comprising the PPAR/RXR heterodimer activator and/or its precursor. The heterodimer activator gets accumulated in the livestock animal.

DETAILED DESCRIPTION - The content of the heterodimer activator or its precursor is at least five, ten or fifteen times the weight of the product fed to the animal. An INDEPENDENT CLAIM is included for improving the quality of carcass and meat of live stock animals, in particular pigs.

USE - To produce livestock product (e.g. skeletal meat, milk and eggs) having increased PPAR/RXR heterodimer activator from livestock animals (e.g. non-ruminant mammals, ruminants, poultry, aquatic animals) for human consumption (claimed).

ADVANTAGE - By supplementing the feed of live stock with **phytanic** acid (PhA) or other PPAR/RXR heterodimer activator provides livestock product with increased levels of the activator to have beneficial effect on the health of humans consuming the livestock product, with lower risk of overload, overdose or adverse effects of the heterodimer activity on the consumers. PhA is used for treatment or prevention of **diabetes**, and treatment of vitamin F deficiency. The branched nature of PhA seriously impeded the activity of several fatty acid enzymes that do not seem impacted as much by conjugated linoleic acid (CLA). PhA inhibits adipose tissue lipoprotein lipase blocking its deposition in fat tissue, and the mammary gland lipoprotein lipase discriminates against PhA in milk, despite high plasma levels. The quality of carcass and meat of live stock animals, in particular pigs is improved. Since PhA is completely saturated it does not exhibit different activities, does not have inherent problem of oxidation, is more stable during storage processing and heating, and does not exhibit endogenous production, compared to CLA.
Dwg.0/0

L8 ANSWER 2 OF 30 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004632823 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15607577
TITLE: Up-regulation of PPARgamma coactivator-1alpha as a strategy for preventing and reversing insulin resistance and obesity.
AUTHOR: McCarty Mark F
CORPORATE SOURCE: NutriGuard Research, 1051 Hermes Ave., Encinitas, CA 92024, USA.. mccarty@pantox.com
SOURCE: Medical hypotheses, (2005) 64 (2) 399-407.
Journal code: 7505668. ISSN: 0306-9877.

Searcher : Shears 571-272-2528

PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20041221
Last Updated on STN: 20050202

AB Excessive accumulation of triglycerides and certain fatty acid derivatives in skeletal muscle and other tissues appears to mediate many of the adverse effects of insulin resistance syndrome. Although fatty diets and obesity can promote such accumulation, deficient capacity for fatty acid oxidation can also contribute in this regard. Indeed, in subjects who are insulin resistant, **diabetic**, and/or obese, fatty acid oxidation by skeletal muscle tends to be inefficient, reflecting decreased expression of mitochondria and mitochondrial enzymes in muscle. This phenomenon is not corrected by weight loss, is not simply reflective of subnormal physical activity, and is also seen in lean first-degree relatives of **diabetics**; thus, it appears to be primarily attributable to genetic factors. Recent studies indicate that decreased expression of PPARgamma coactivator-1alpha (PGC-1alpha), a "master switch" which induces mitochondrial biogenesis by supporting the transcriptional activity of the nuclear respiratory factors, may largely account for the diminished oxidative capacity of subjects prone to insulin resistance. Thus, feasible measures which up-regulate PGC-1alpha may be useful for preventing and treating insulin resistance and obesity. These may include exercise training, metformin and other agents which stimulate AMP-activated kinase, high-dose biotin, and PPARdelta agonists. Drugs which are specific agonists for PPARdelta show remarkable efficacy in rodent models of insulin resistance, **diabetes**, and obesity, and are currently being evaluated clinically. **Phytanic** acid, a branched-chain fatty acid found in omnivore diets, can also activate PPARdelta, and thus should be examined with respect to its impact on mitochondrial biogenesis and insulin sensitivity.

L8 ANSWER 3 OF 30 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004562288 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15533633
TITLE: Nutraceutical resources for **diabetes** prevention--an update.
AUTHOR: McCarty Mark F
CORPORATE SOURCE: NutriGuard Research, 1051 Hermes Avenue, Encinitas, CA 92024, USA.. mccarty@pantox.com
SOURCE: Medical hypotheses, (2005) 64 (1) 151-8. Journal code: 7505668. ISSN: 0306-9877.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20041110
Last Updated on STN: 20041230

AB There is considerable need for safe agents that can reduce risk for **diabetes** in at-risk subjects. Although certain drugs--including metformin, acarbose, and orlistat--have shown **diabetes** -preventive activity in large randomized studies, nutraceuticals have potential in this regard as well. Natural agents which slow carbohydrate absorption may mimic the protective effect of acarbose; these include: soluble fiber--most notably glucomannan; chlorogenic acid--likely

responsible for reduction in **diabetes** risk associated with heavy coffee intake; and legume-derived alpha-amylase inhibitors. There does not appear to be a natural lipase inhibitor functionally equivalent to orlistat, although there are poorly documented claims for Cassia nomame extracts. Metformin's efficacy reflects activation of AMP-activated kinase; there is preliminary evidence that certain compounds in barley malt have similar activity, without the side effects associated with metformin. In supraphysiological concentrations, biotin directly activates soluble guanylate cyclase; this implies that, at some sufficient intake, biotin should exert effects on beta cells, the liver, and skeletal muscle that favor good glucose tolerance and maintenance of effective beta cell function. Good magnesium status is associated with reduced **diabetes** risk and superior insulin sensitivity in recent epidemiology; ample intakes of chromium picolinate appear to promote insulin sensitivity in many individuals and improve glycemic control in some **diabetics**; calcium/vitamin D may help preserve insulin sensitivity by preventing secondary hyperparathyroidism. Although conjugated linoleic acid--like thiazolidinediones, a PPAR-gamma agonist--has not aided insulin sensitivity in clinical trials, the natural rexinoid **phytanic** acid exerts thiazolidinedione-like effect in animals and cell cultures, and merits clinical examination. Other natural agents with the potential to treat and possibly prevent **diabetes** include extracts of bitter melon and of cinnamon. Nutraceuticals featuring meaningful doses of combinations of these agents would likely have substantial **diabetes**-preventive efficacy, and presumably could be marketed legally as aids to good glucose tolerance and insulin sensitivity.

L8 ANSWER 4 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:396833 BIOSIS
DOCUMENT NUMBER: PREV200400402240
TITLE: **Phytanic** acid derivative compositions.
AUTHOR(S): Fluehmann, Beat [Inventor, Reprint Author]; Hunziker, Willi [Inventor]
CORPORATE SOURCE: Zurich, Switzerland
ASSIGNEE: Roche Vitamins Inc.
PATENT INFORMATION: US 6784207 August 31, 2004
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug 31 2004) Vol. 1285, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Oct 2004
Last Updated on STN: 13 Oct 2004

AB The present invention is a method for the treatment or prevention of preferably **non-insulin dependent** (**NIDDM** or so-called **Type II**) **diabetes** mellitus, or other conditions associated with impaired glucose tolerance such as obesity, and in particular to the use of **phytanic** acid derivatives for the said treatment and/or prevention. A method of making a composition for the treatment or prevention of **non-insulin dependent diabetes** mellitus and related diseases comprising combining **phytanic** acid or derivatives thereof with a pharmaceutically acceptable additive or

adjuvant, and a composition for the treatment or prevention of **non -insulin dependent diabetes** mellitus comprising **phytanic** acid or derivatives thereof are also provided.

L8 ANSWER 5 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-580630 [56] WPIDS
CROSS REFERENCE: 2004-580605 [56]
DOC. NO. CPI: C2004-211625
TITLE: Use of a composition comprising acid derivatives for the treatment of diseases or illness e.g. **diabetes**, obesity, inflammation, cystic fibrosis and dementia.
DERWENT CLASS: B05
INVENTOR(S): GUTIERREZ, I; MURRAY, E D; SCHWARTZ, E B; WECHTER, W J; GUITERREZ, I; MURRAY, D E
PATENT ASSIGNEE(S): (GUTI-I) GUTIERREZ I; (MURR-I) MURRAY E D; (SCHW-I) SCHWARTZ E B; (WECH-I) WECHTER W J; (ENCO-N) ENCORE PHARM INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004064761	A2	20040805	(200456)*	EN	59
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
US 2004152777	A1	20040805	(200456)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004064761	A2	WO 2004-US1698	20040121
US 2004152777	A1 Provisional	US 2003-441892P	20030122
		US 2004-762681	20040121

PRIORITY APPLN. INFO: US 2003-441892P 20030122; US 2004-762681 20040121
AN 2004-580630 [56] WPIDS
CR 2004-580605 [56]
AB WO2004064761 A UPAB: 20040901
NOVELTY - Treatment of diseases or illness comprises administration of a composition comprising acid derivatives (I) and their stereochemical configuration of the alpha carbon is predominantly R-stereoisomer or R-stereoisomer substantially free from the S-stereoisomer having elicit chemopreventative effect, therapeutic effect, prophylactic effect or chemoprotective effect.

DETAILED DESCRIPTION - Treatment of diseases or illness comprises administration of a composition comprising acid derivatives of formula (I) (A-CH(D)-CO2H (A) or W-C(X)(D)-CO2H (B)) and their stereochemical

configuration of the alpha carbon is predominantly R-stereoisomer or R-stereoisomer substantially free from the S-stereoisomer having elicit a chemopreventative effect or therapeutic effect or a prophylactic effect or a chemoprotective effect.

A = optionally substituted 3-30C alkyl or 3-30C alkene having 1-10 unsaturation or 3-30C alkyne having 1-10 unsaturation;

X = 1-10C alkyl;

W = optionally substituted 1-30C alkyl or 2-30C alkene having 1-10C unsaturation; and

D = 1-10C alkyl.

ACTIVITY - Antidiabetic; Anorectic; Antiinflammatory; CNS-Gen.; Respiratory-Gen.; Nootropic; Cytostatic.

MECHANISM OF ACTION - None given.

USE - (I) is useful for the treatment of disease or illness e.g. **diabetes**, obesity, inflammation, cystic fibrosis, dementia or neoplastic disease in human (claimed).

ADVANTAGE - (I) should be compatible with the digestive processes of humans.

Dwg.0/1

L8 ANSWER 6 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-561686 [54] WPIDS
DOC. NO. CPI: C2004-205225
TITLE: Composition used in preparation of emulsions comprises phospholipids enriched in polyunsaturated fatty acids, mono-terpenes and at least one tryptophan and/or phytol derivative.
DERWENT CLASS: B05 D13 E19
INVENTOR(S): PISTOLESI, E
PATENT ASSIGNEE(S): (HUNZ-N) HUNZA DI PISTOLESI ELVIRA & C SAS
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004062389	A1	20040729	(200454)*	EN	16

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004062389	A1	WO 2004-EP66	20040108

PRIORITY APPLN. INFO: IT 2003-MI36 20030113
AN 2004-561686 [54] WPIDS
AB WO2004062389 A UPAB: 20040823
NOVELTY - Composition comprises phospholipids enriched in polyunsaturated fatty acids, mono-terpenes and at least one tryptophan and/or phytol

derivative.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparation of an emulsion which comprising inverted micelles, which comprises:

(a) dissolving the phospholipid(s), the phytol and tryptophan derivative(s) in organic apolar solvents, followed by solvent evaporation;

(b) spraying essential oil(s) containing the monoterpene(s) on the powder obtained in (a); and

(c) dissolving the sprayed powder in polyunsaturated oil(s).

ACTIVITY - Dermatological; Anorectic; Antiarteriosclerotic; Antidiabetic; Hypotensive; Antilipemic; Nootropic; Neuroprotective; Antiparkinsonian; Osteopathic; Tranquilizer; Antidepressant; Gynecological; Endocrine-Gen..

MECHANISM OF ACTION - None given.

USE - Used for the preparation of an emulsion containing inverted micelles (claimed) useful for the prevention of aging, obesity, overweight, atherosclerosis, **diabetes**, hypertension, dyslipidemia, Alzheimer's disease, Parkinson's disease, senile dementia, osteoporosis, mental and physical stress, depression, menopausal disorders, prostate hypertrophy, skin aging, alopecia and cellulitis.

ADVANTAGE - The composition shows improved bioavailability, stability and organoleptic properties.

Dwg.0/0

L8 ANSWER 7 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-400528 [37] WPIDS

DOC. NO. CPI: C2004-149980

TITLE: Composition useful in the treatment of type 1 and 2 **diabetes** comprises at least two components selected from epigallocatechin gallate (EGCG), pantethine or its metabolite, **phytanic** acid, lipoic acid and coenzyme Q-10..

DERWENT CLASS: B02 B05 D13

INVENTOR(S): RAEDERSTORFF, D; TEIXEIRA, S R; WEBER, P

PATENT ASSIGNEE(S): (STAM) DSM IP ASSETS BV

COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004041257	A2	20040521	(200437)*	EN	21
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003293592	A1	20040607	(200469)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004041257	A2	WO 2003-EP10838	20030930
AU 2003293592	A1	AU 2003-293592	20030930

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003293592	A1 Based on	WO 2004041257

PRIORITY APPLN. INFO: EP 2002-24804 20021107
AN 2004-400528 [37] WPIDS
AB WO2004041257 A UPAB: 20040611
NOVELTY - A composition comprises at least two components selected from epigallocatechin gallate (EGCG), pantethine or its metabolite, **phytanic** acid, lipoic acid, coenzyme Q-10 and optionally policosanol.
ACTIVITY - Antidiabetic; Anorectic.
MECHANISM OF ACTION - None given.
USE - As food or beverage or supplement composition for a food or beverage; in the manufacture of nutraceutical composition useful in the treatment of type 1 and 2 **diabetes** and for the prevention of **type 2 diabetes** in the individuals with pre-**diabetes**, impaired glucose tolerance or obesity (claimed).
ADVANTAGE - The composition provides additive and/or synergetic effects.
Dwg.0/0

L8 ANSWER 8 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-389736 [36] WPIDS
DOC. NO. CPI: C2004-146044
TITLE: New beta-ionol derivatives, useful for beautifying mammalian skin and for treating cancer, allergic dermatitis, contact dermatitis, lymphoma and **diabetes**.
DERWENT CLASS: B05
INVENTOR(S): BIEDERMANN, K A; BISSETT, D L; BOYER, A S; COHEN, S L; DELONG, M A; SNIDER, C E
PATENT ASSIGNEE(S): (PROC) PROCTER & GAMBLE CO
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004037213	A2	20040506	(200436)*	EN	83
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
US 2004131648	A1	20040708	(200445)		
AU 2003285042	A1	20040513	(200468)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2004037213	A2	WO 2003-US34155	20031023
US 2004131648	A1	US 2002-279397	20021024
AU 2003285042	A1	AU 2003-285042	20031023

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003285042	A1 Based on	WO 2004037213

PRIORITY APPLN. INFO: US 2002-279397 20021024

AN 2004-389736 [36] WPIDS

AB WO2004037213 A UPAB: 20040608

NOVELTY - Beta-ionol derivatives (I)-(IV) are new.

DETAILED DESCRIPTION - Beta-ionol derivatives of formula (I)-(IV) are new.

For (I):

X = single or double bonded moiety comprising 0-12 optionally substituted carbon atoms; 0-2 heteroatoms, selected from optionally substituted cycloalkyl and aromatic moieties of NH, S and/or O (sic);

Z = a single, double, or triple bonded moiety containing 0-12 carbon atoms in a chain, optionally including a cycloalkyl or aromatic ring, both of which may be further substituted;

Y = (CH2)n';

n' = 0-3;

R = a group which may be substituted onto any ring if two or more are present and is selected from no greater than three optionally substituted, alkyl, cycloalkyl or aromatic moieties including CH3, CH2CH3, NR1R2, SR asterisk and/or OR asterisk

N.B. R asterisk , R1 and R2 are not defined.

For (II):

X = heteroatom selected from optionally substituted O, N and S, where O, N and S may be singly- or doubly bonded to the molecule, provided that when the heteroatom is doubly bonded, then there is no R2;

R1-R4 = H; optionally substituted lower alkyl chain of 0-6 member atoms, monocyclic, bicyclic and aromatic rings; .

provided that neither R1 nor R2 may be methyl or hydrogen when X is a hydroxyl moiety; and

provided that when X is allylic, R1 may not be H when R2 is lower alkyl, phenyl or alkynyl.

For (III):

X = heteroatom selected from optionally substituted N, O, P and/or S, where N, O, P and S may be singly- or doubly bonded to the molecule, provided that when the heteroatom is doubly bonded, then there is no R2

R1, R2 = H, lower alkyl chain of 0-6 member atoms, monocyclic, bicyclic, and aromatic rings, where the member atoms are optionally substituted;

provided that R1 and R2 may not simultaneously be H or methyl when X is OH, and that R1 is H when X is O in the absence of R2;

R3-R6 = H, lower alkyl chain of 0-6 member atoms, monocyclic, bicyclic, and aromatic rings, where the member atoms are optionally substituted, provided that R3 is not methyl and that R4 and R5 are not simultaneously methyl.

For (IV):

X = CH2, or a heteroatom selected from N, O, S optionally substituted and singly or doubly bonded to the molecule, provided that when the

heteroatom is doubly bonded, then there is no R2; and
provided that:

when X is a ketone moiety and R3 and R4 are simultaneously H, then R1 may not be H, Me, ethyl, CH2CH2Cl, CH2BrMe, OH, CH2NH2, CH2CHPh, (CO)Me or (CO)Ph;

when X is OH and R2, R3 and R4 are simultaneously H, then R1 may not be ethyl or (CO)OEt;

R1, R2 = H, lower alkyl chain of 0-6 member atoms, monocyclic, bicyclic, and aromatic rings, where the member atoms are optionally substituted;
provided that:

(1) R1 and R2 may not be optionally substituted aniline moieties;

(2) R1 and R2 may not both be aromatic rings;

(3) R1 and R2 may not be, contain, be substituted by, or be contained within nitrogen containing rings, and may not be joined in a ring with X via an ester linkage;

(4) R1 and R2 may not contain an acid anhydride moiety;

R3, R4 = H, lower alkyl chain of 0-6 member atoms, monocyclic, and aromatic rings, where the member atoms may not be substituted;
provided that:

(5) when X is a double bonded O, R1, R3, and R7-R14 are H, and R5, R6, R15, R16 are Me, then R4 cannot be H, OH, OMe, or OCH2OMe;

(6) when X is a double bonded O, R1, R3, and R5-R16 are H, then R4 cannot be H, OH, OMe, OEt, OPh, or OAc; and in such instance if R1 is Me and R3 is OH, then R4 cannot be Me, CF3, Ph, or CH2CH2Ph;

R5-R16 = H, lower alkyl chain of 0-3 member atoms;
provided that:

(7) R5-R16 may not represent moieties that produce unstable compounds;

(8) when R5-R10 and R13-R16 are H, then R11 and R12 may not combine to form a ketone; and

any geminal group of R5-R16 may be combined to form a cyclopropyl moiety or an exocyclic methylene

INDEPENDENT CLAIMS are also included for the following:

(1) fatty acid analogs of formula (B); and

(2) a mixture (P) comprising 0.001-99.99 % (I) and 99.99-0.001% (B);

(3) a fatty acid analog for the beautification of mammalian skin;

(4) beautifying mammalian skin, slowing the deterioration of mammalian skin, and reducing the loss of function of mammalian skin comprising topical application of (I)-(IV) and (B).

R = a group of formula (a);

A = H, methyl and ethyl;

m, n, o, p = 0-8; and

where methylene groups are optionally saturated, optionally substituted, and/or a constituent of a ring structure.

ACTIVITY - Cytostatic; Dermatological; Gastrointestinal-Gen.; Antidiabetic; Antiallergic.

Test details are described but no results are given.

MECHANISM OF ACTION - (I)-(IV) are RXR, RAR and/or PPAR nuclear hormone receptor ligands.

(RXR = retinoid X receptor; RAR = retinoic acid receptor; PPAR = peroxisome proliferator-activated receptor).

USE - (I)-(IV) reduce the loss of function and deterioration, differentiation and/or proliferation of RXR-containing mammalian tissue. (I)-(IV) and their mixtures with the fatty acid analogs are useful for treating cancer, allergic dermatitis, contact dermatitis, lymphoma,

diabetes, gastrointestinal or skin disorders. The compounds and mixtures are also useful for beautifying mammalian skin, where beautifying means removing fine lines, removing wrinkles, repairing photo damaged skin, repairing aged skin, improving skin surface texture, reducing skin hyperpigmentation, improving skin sagging, and/or repairing damage from disease, where the disease is allergic dermatitis, contact dermatitis, lymphoma, diabetes and/or gastrointestinal disorders (all claimed).

ADVANTAGE - Notable synergy is achieved via the combined administration of 2 or more analogs from the same or different groups of (I)-(IV). Synergy is also achieved via the combined employment of (I)-(IV) and the fatty acid analogs. Unlike prior art products which are appearance-concealing (e.g. color cosmetics), the compounds actually improve the condition of mammalian skin.

Dwg.0/0

L8 ANSWER 9 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-226712 [21] WPIDS

DOC. NO. CPI: C2004-089383

TITLE: Nutraceutical compositions, useful to treat/prevent **diabetes** and other conditions associated with impaired glucose tolerance, comprise biotin and pantethine, epigallocatechin gallate, **phytanic** acid, lipoic acid and/or policosanol.

DERWENT CLASS: B05 D13

INVENTOR(S): EGGERSDORFER, M L; RAEDERSTORFF, D; TEIXEIRA, S R; WEBER, P

PATENT ASSIGNEE(S): (STAM) DSM IP ASSETS BV

COUNTRY COUNT: 100

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004017766	A1	20040304	(200421)*	EN	32
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
AU 2003266287	A1	20040311	(200457)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004017766	A1	WO 2003-EP9112	20030818
AU 2003266287	A1	AU 2003-266287	20030818

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003266287	A1 Based on	WO 2004017766

PRIORITY APPLN. INFO: EP 2003-14625 20030626; EP 2002-18847 20020823

AN 2004-226712 [21] WPIDS
AB WO2004017766 A UPAB: 20040326
NOVELTY - Composition (I) comprises biotin in an amount that provides a daily dosage of 0.01-3 mg/kg and at least one additional component (i.e. pantethine or its metabolite, epigallocatechin gallate (EGCG), **phytanic** acid, lipoic acid and/or policosanol) (A).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a food or beverage comprising about 0.03-50 mg of biotin per serving and (A).

ACTIVITY - Antidiabetic; Anorectic; Analgesic; Antianginal.

The antidiabetic efficacy of (I) was tested in mice using a combination of biotin and **phytanic** acid, while the control group received either biotin alone or **phytanic** acid alone. Determination of blood glucose levels after treatment showed that combined treatment with biotin and **phytanic** acid exerted a synergistic effect with 25.9% and 33.2% glucose removal rate (GRR) at 90 and 180 minutes respectively, as compared to 11.6% + 9.7% (21.3%) and 15% + 15.2% (30.2%) for the controls.

MECHANISM OF ACTION - None given in the source material.

USE - (I) is useful as a nutraceutical composition for the treatment of type 1 **diabetes** mellitus, treatment /prevention of **type 2 diabetes** in individuals with pre-**diabetes**, impaired glucose tolerance (IGT) or obesity and for the treatment of other conditions associated with IGT such as syndrome X and obesity.

ADVANTAGE - (I) comprises components that have different mechanisms of action on glucose metabolism and insulin sensitivity, thus providing additive and/or synergetic effects in the treatment of **diabetes**. (I) also provides a safe and effective nutritional supplement with minimal side effects.

Dwg.0/0

L8 ANSWER 10 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-643105 [63] WPIDS
DOC. NO. CPI: C2004-231310
TITLE: Use of **phytanic** acid for treating **diabetes**.
DERWENT CLASS: B05
INVENTOR(S): ZHOU, D
PATENT ASSIGNEE(S): (BEIY-N) BEIYI MEDICINE SCI & TECH CO LTD SHANGHA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CN 1507871	A	20040630	(200463)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CN 1507871	A	CN 2002-154971	20021216

PRIORITY APPLN. INFO: CN 2002-154971 20021216
AN 2004-643105 [63] WPIDS

AB CN 1507871 A UPAB: 20041001
NOVELTY - The present invention relates to an application of **phytanic** acid for curing **diabetes**. Said invented medicine is prepared by adopting **phytanic** acid or its derivative and pharmaceutically-acceptable additive and/or adjuvant. The described derivative includes salts with alkali metal and alkali earth metal or their pharmaceutically-acceptable solvent compound. The tests show that said invented medicine has good therapeutic effect for **diabetic**, specially, for patient with hyperglycemia, hyperlipemia and hypertension.
Dwg.0/0

L8 ANSWER 11 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-636002 [62] WPIDS
DOC. NO. CPI: C2004-228670
TITLE: Treating **diabetes** comprises **phytanic** acid or its derivative.
DERWENT CLASS: B04
INVENTOR(S): ZHOU, D
PATENT ASSIGNEE(S): (SHAN-N) SHANGHAI BEIYI MEDICINE SCI TECH CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CN 1506049	A	20040623	(200462)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CN 1506049	A	CN 2002-150936	20021205

PRIORITY APPLN. INFO: CN 2002-150936 20021205
AN 2004-636002 [62] WPIDS
AB CN 1506049 A UPAB: 20041011
NOVELTY - The medicine for treating **diabetes** and its complication is compounded with **phytanic** acid or its derivative, pharmaceutically acceptable additive and/or assistant. The derivative may be alkali metal salt or alkali earth metal salts of **phytanic** acid or their pharmaceutically acceptable solution. Experiment shows that **phytanic** acid and its derivative have the activity of raising the taking of liver glucose and eliminating serum glucose and the activity is expressed by gene in enzyme inducing or stimulating insulin secretion. The present invention has excellent curative effect on **diabetes**, especially **diabetes** companied with hyperlipidemia, hypercholesterolemia, hypertension, obesity and hyperinsulinemia.
Dwg.0/0

L8 ANSWER 12 OF 30 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004140630 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15032732
TITLE: Retinoids and retinoid receptors in the control of energy balance: novel pharmacological strategies in obesity and **diabetes**.
AUTHOR: Villarroya F; Iglesias R; Giralt M

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Barcelona Avda Diagonal 645, E-08028-Barcelona, Spain.. gombau@bio.ub.es
SOURCE: Current medicinal chemistry, (2004 Mar) 11 (6) 795-805. Ref: 131
Journal code: 9440157. ISSN: 0929-8673.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040323
Last Updated on STN: 20040528
Entered Medline: 20040527

AB Obesity and **type II diabetes** are closely related metabolic diseases with an increasing incidence worldwide. No clear-cut pharmacological treatment for these complex metabolic disturbances is available despite current efforts. New directions and perspectives for the pharmacological or nutritional treatment of these diseases should be defined. In recent years, a growing body of evidence shows that retinoids and retinoic acid receptors are involved in the control of biological aspects (e.g. adiposity and energy expenditure mechanisms), which offers great potential for research on the treatment of obesity and **type II diabetes**. All-trans retinoic acid is known to inhibit adipocyte differentiation, whereas, molecules activating the retinoid X-receptor (rexinoids) promote the differentiation of adipocytes. Treatment with rexinoids ameliorates glycemic control in rodent models of **type II diabetes** and obesity, although other findings indicate similar positive effects by inhibiting the receptor. Moreover, natural products of dietary origin, such as **phytanic** acid can activate RXR and thus, trigger adipose cell differentiation. Finally, the activation of retinoic acid receptors or retinoid X receptors has been reported to induce the gene expression of uncoupling proteins, which are mitochondrial proteins involved in the regulation of energy expenditure and fatty acid metabolism. Further research is required to exploit the capacities of the retinoid-dependent pathways of regulation of adiposity, insulin sensitivity and energy expenditure for drug development in metabolic disturbances.

L8 ANSWER 13 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004518203 EMBASE
TITLE: Diet, fatty acids, and regulation of genes important for heart disease.
AUTHOR: Vanden Heuvel J.P.
CORPORATE SOURCE: Dr. J.P. Vanden Heuvel, Department of Veterinary Sciences, Ctr. Molec. Toxicol./Carcinogenesis, Pennsylvania State University, 226 Fenske Laboratory, University Park, PA 16802, United States. jpv2@psu.edu
SOURCE: Current Atherosclerosis Reports, (2004) 6/6 (432-440). Refs: 85
ISSN: 1523-3804 CODEN: CARUCZ
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Diets rich in omega-3 polyunsaturated fatty acids (n-3 PUFAs), such as alpha-linoleic acid, eicosapentaenoic acid, and docosahexaenoic acid, are associated with decreased incidence and severity of coronary heart disease. Similarly, conjugated linoleic acids (CLAs), which are found in meat and dairy products, have beneficial effects against atherosclerosis, **diabetes**, and obesity. The effects of n3-PUFAs and CLAs are in contrast to fatty acids with virtually identical structures, such as linoleic acid and arachidonic acid (ie, n-6 PUFAs). This article discusses the possibility that cognate receptors exist for fatty acids or their metabolites that are able to regulate gene expression and coordinately affect metabolic or signaling pathways associated with coronary heart disease. Three nuclear receptors are emphasized as fatty acid receptors that respond to dietary and endogenous ligands: peroxisome proliferator activated receptors, retinoid X receptors, and liver X receptors.

L8 ANSWER 14 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:288048 BIOSIS
DOCUMENT NUMBER: PREV200400286805
TITLE: Induction of Inflammatory Markers in Epididymal Adipose Tissue of Diet-Induced Obese (DIO) C57BL/6J Mice: Impact of **Phytanic** Acid and BRL49653.
AUTHOR(S): Teixeira, Sandra R [Reprint Author]; Preller, Mareike; Wang, Ying; Schwager, Joseph; Champy, Marie-France; Auwerx, Johan; Elste, Volker; Weber, Peter; Fluehmann, Beat
CORPORATE SOURCE: R&&AMPD Human Nutrition and Health, DSM Nutritional Products, P.O: Box 3255, Bldg 205/209B, Basel, 4002, Switzerland
sandra-renata.teixeira@dsm.com
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 356.13. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB The innate immune system and the stimulation of acute-phase protein synthesis in liver have been postulated to contribute to insulin resistance and T2DM. In this study, we examined the effect of diet-induced obesity on gene expression of inflammatory markers in adipose tissue. 48 male C57BL/6J mice were assigned to 4 groups (n=12/group). One group received chow (lean control, LC), while 3 groups received a high-fat (HF) diet. One of the HF groups served as the fat control (FC), whereas the other 2 received additionally either **phytanic** acid at 150 mpk or BRL49653 at 10 mpk (TZD). Mice receiving HF became obese and

diabetic during the study period. After 23wks, epididymal adipose tissue was collected from 6 mice/group and analyzed using Affymetrix Genechip. Genes known to be involved in inflammatory responses were selected and further filtered to include only those with change factors <-0.5 or >0.5 and p-value <0.05. HF diet resulted in upregulation of the acute-phase proteins haptoglobin, and orosomucoid 1 and 2, the lipopolysaccharide (LPS) binding protein, and heat-shock protein (HSP) 72. Treatment with either PPARgamma agonist resulted in a downregulation of the expression of most of these markers to levels close to LC. Other classical inflammatory markers were not regulated. Our results with selected inflammatory markers suggest that diet-induced obesity induces a persistent acute-phase reaction in adipose tissue, which may contribute to insulin-resistance. Moreover, the two investigated PPARgamma agonists can reduce the amount of inflammation, while improving metabolic status.

L8 ANSWER 15 OF 30 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:1079747 SCISEARCH
THE GENUINE ARTICLE: 748YJ
TITLE: Bitter gourd (Momordica charantia) extract activates peroxisome proliferator-activated receptors and upregulates the expression of the acyl CoA oxidase gene in H4IIEC3 hepatoma cells
AUTHOR: Chao C Y; Huang C J (Reprint)
CORPORATE SOURCE: Natl Taiwan Univ, Dept Biochem Sci & Technol, Lab Nutr Biochem, 1 Roosevelt Rd, Sec 4, Taipei 104, Taiwan (Reprint); Natl Taiwan Univ, Dept Biochem Sci & Technol, Lab Nutr Biochem, Taipei 104, Taiwan; Natl Taiwan Univ, Inst Microbiol & Biochem, Taipei 104, Taiwan
COUNTRY OF AUTHOR: Taiwan
SOURCE: JOURNAL OF BIOMEDICAL SCIENCE, (15 DEC 2003) Vol. 10, No. 6, Part 2, pp. 782-791.
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 1021-7770.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Peroxisome proliferator-activated receptor alpha (PPARalpha) is a ligand-dependent transcription factor that regulates the expression of genes involved in lipid metabolism and transport. Ligands/activators of PPARalpha, like fibrate-type drugs, may have hypolipidemic effects. To identify food that contains activators of PPARalpha, a transactivation assay employing a clone of CHO-K1 cells stably transfected with a (UAS)(4)-tk-alkaline phosphatase reporter and a chimeric receptor of Gal4-rPPARalpha LBD was used to screen ethyl acetate (EA) extracts of a large variety of food materials. It was found that the EA extract of bitter gourd (Momordica charantia), a common oriental vegetable, activated PPARalpha to an extent that was equivalent to or even higher than 10 muM Wy-14643, a known ligand of PPARalpha. This extract also activated PPARgamma to a significant extent which was comparable to 0.5 muM BRL-49653. The activity toward PPARalpha was mainly in the soluble fraction of the organic solvent. The EA extract prepared from the whole fruit showed significantly higher activity than that from seeds or flesh alone. The bitter gourd EA extract was then incorporated into the medium

for treatment of a peroxisome proliferator-responsive murine hepatoma cell line, H4IIEC3, for 72 h. Treated cells showed significantly higher activity of acyl CoA oxidase and higher expressions of mRNA of this enzyme and fatty acid-binding protein, indicating that the bitter gourd EA extract was able to act on a natural PPARalpha signaling pathway in this cell line. It is thus worth further investigating the PPAR-associated health benefits of bitter gourd. Copyright (C) 2003 National Science Council, ROC and S. Karger AG, Basel.

L8 ANSWER 16 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003409284 EMBASE
TITLE: Reviews: Current topics role of nuclear receptors in the regulation of gene expression by dietary fatty acids (review).
AUTHOR: Khan S.A.; Vanden Heuvel J.P.
CORPORATE SOURCE: J.P. Vanden Heuvel, Department of Veterinary Science, Ctr. Molec. Toxicol./Carcinogenesis, Penn State University, University Park, PA 16802, United States. jpv2@psu.edu
SOURCE: Journal of Nutritional Biochemistry, (1 Oct 2003) 14/10 (554-567).
Refs: 142
ISSN: 0955-2863 CODEN: JNBIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Long chain fatty acids, derived either from endogenous metabolism or by nutritional sources play significant roles in important biological processes of membrane structure, production of biologically active compounds, and participation in cellular signaling processes. Recently, the structure of dietary fatty acids has become an important issue in human health because ingestion of saturated fats (containing triglycerides composed of saturated fatty acids) is considered harmful, while unsaturated fats are viewed as beneficial. It is important to note that the molecular reason for this dichotomy still remains elusive. Since fatty acids are important players in development of pathology of cardiovascular and endocrine system, understanding the key molecular targets of fatty acids, in particular those that discriminate between saturated and unsaturated fats, is much needed. Recently, insights have been gained on several fatty acid-activated nuclear receptors involved in gene expression. In other words, we can now envision long chain fatty acids as regulators of signal transduction processes and gene regulation, which in turn will dictate their roles in health and disease. In this review, we will discuss fatty acid-mediated regulation of nuclear receptors. We will focus on peroxisome proliferators-activated receptors (PPARs), liver X receptors (LXR), retinoid X receptors (RXRs), and Hepatocyte Nuclear Factor alpha (HNF-4α), all of which play pivotal roles in dietary fatty acid-mediated effects. Also, the regulation of gene expression by Conjugated Linoleic Acids (CLA), a family of dienoic fatty acids with a variety of beneficial effects, will be discussed. .COPYRGT. 2003 Elsevier Inc. All rights reserved.

L8 ANSWER 17 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN
ACCESSION NUMBER: 2003103483 EMBASE
TITLE: **Phytanic** acid alpha-oxidation, new insights into an old problem: A review.
AUTHOR: Wanders R.J.A.; Jansen G.A.; Lloyd M.D.
CORPORATE SOURCE: R.J.A. Wanders, Depts. Pediat./Emma Children's H., Academic Medical Centre, University Hospital Amsterdam, P.O. Box 22700, 1100 DE Amsterdam, Netherlands. r.j.wanders@amc.uva.nl
SOURCE: Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, (17 Mar 2003) 1631/2 (119-135). Refs: 91 ISSN: 1388-1981 CODEN: BBMLFG
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Phytanic** acid (3,7,10,14-tetramethylhexadecanoic acid) is a branched-chain fatty acid which is known to accumulate in a number of different genetic diseases including Refsum disease. Due to the presence of a methyl-group at the 3-position, **phytanic** acid and other 3-methyl fatty acids can not undergo β-oxidation but are first subjected to fatty acid α-oxidation in which the terminal carboxyl-group is released as CO(2). The mechanism of α-oxidation has long remained obscure but has been resolved in recent years. Furthermore, peroxisomes have been found to play an indispensable role in fatty acid α-oxidation, and the complete α-oxidation machinery is probably localized in peroxisomes. This Review describes the current state of knowledge about fatty acid α-oxidation in mammals with particular emphasis on the mechanism involved and the enzymology of the pathway. .COPYRGT. 2003 Elsevier Science B.V. All rights reserved.

L8 ANSWER 18 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-270864 [32] WPIDS
DOC. NO. CPI: C2002-080448
TITLE: New composition comprising **phytanic** acid or its derivatives, useful for treating or preventing **non-insulin dependent** **diabetes** mellitus, impaired glucose tolerance and related obesity.
DERWENT CLASS: B04
INVENTOR(S): FLUEHAMNN, B; HEIM, M; HUNZIKER, W; WEBER, P; FLUEHMANN, B
PATENT ASSIGNEE(S): (HOFF) ROCHE VITAMINS AG; (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE VITAMINS INC
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1177789	A2	20020206	(200232)*	EN	29
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001003209	A	20020326	(200232)		

CA 2353805	A1	20020204	(200232)	EN
JP 2002104964	A	20020410	(200240)	11
US 2002082298	A1	20020627	(200245)	
KR 2002011926	A	20020209	(200257)	
CN 1365667	A	20020828	(200282)	
US 2004138181	A1	20040715	(200447)	
US 6784207	B2	20040831	(200457)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1177789	A2	EP 2001-118230	20010730
BR 2001003209	A	BR 2001-3209	20010803
CA 2353805	A1	CA 2001-2353805	20010803
JP 2002104964	A	JP 2001-233070	20010801
US 2002082298	A1	US 2001-915152	20010725
KR 2002011926	A	KR 2001-46946	20010803
CN 1365667	A	CN 2001-124878	20010803
US 2004138181	A1 Div ex	US 2001-915152	20010725
		US 2004-766118	20040127
US 6784207	B2	US 2001-915152	20010725

PRIORITY APPLN. INFO: EP 2000-116848 20000804

AN 2002-270864 [32] WPIDS

AB EP 1177789 A UPAB: 20020829

NOVELTY - A composition for treating or preventing **non-insulin dependent diabetes** mellitus comprising **phytanic** acid or its derivatives, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing a product for the treatment or prevention of a disease such as **non-insulin dependent diabetes** mellitus, syndrome X, hyperlipidemia, hypertension, hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, impaired glucose tolerance and related obesity, by combining **phytanic** acid or its derivatives, with a pharmaceutical carrier;

(2) a dietary supplement comprising the new composition;

(3) treating or preventing **diabetes** mellitus, and conditions associated with **diabetes** mellitus in a human or animal, by administering the composition or the dietary supplement comprising **phytanic** acid, a **phytanic** acid precursor, or a derivative of **phytanic** acid; and

(4) increasing cellular glucose uptake by administering a **phytanic** acid derivative or **phytanic** acid precursor.

ACTIVITY - Antidiabetic; antilipemic; hypotensive; anorectic.

No supporting data available.

MECHANISM OF ACTION - Glucokinase modulator.

No supporting data available.

USE - The **phytanic** acid or their derivatives or precursors are useful as pharmaceutical compounds or supplements to foods or feeds for the treatment or prevention of **type II** or **non-insulin dependent diabetes** mellitus, hyperlipidemia, hypertension, hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, impaired glucose tolerance and

related obesity (all claimed). **Phytanic** or its derivatives are also useful in insulin therapy in combination with known active compounds. Dwg.0/7

L8 ANSWER 19 OF 30 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002430313 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12187408
TITLE: The chlorophyll-derived metabolite **phytanic** acid induces white adipocyte differentiation.
AUTHOR: Schluter A; Yubero P; Iglesias R; Giralt M; Villarroya F
CORPORATE SOURCE: Department de Bioquimica i Biologia Molecular, Universitat de Barcelona, Spain.
SOURCE: International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, (2002 Sep) 26 (9) 1277-80.
Journal code: 9313169. ISSN: 0307-0565.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20020821
Last Updated on STN: 20030306
Entered Medline: 20030305

AB **Phytanic** acid is a derivative of the phytol side-chain of chlorophyll. It appears in humans following the ingestion of fat-containing foods and is present in human blood at a low micromolar concentration. It may activate retinoid X receptors (RXR) or peroxisome proliferator-activated receptor (PPAR) alpha in vitro. **Phytanic** acid induced the adipocyte differentiation of 3T3-L1 cells in culture as assessed by accumulation of lipid droplets and induction of the aP2 mRNA marker. This effect was mimicked by a synthetic activator of RXR but not by a PPARalpha agonist or by palmitic acid. In human pre-adipocytes in primary culture, **phytanic** acid also induced adipocyte differentiation. These findings indicate that **phytanic** acid may act as a natural rexinoid in adipose cells and suggest a potential use in the treatment of human **type 2 diabetes** and obesity.

L8 ANSWER 20 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2002242714 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11923221
TITLE: **Phytanic** acid, a natural peroxisome proliferator-activated receptor (PPAR) agonist, regulates glucose metabolism in rat primary hepatocytes.
AUTHOR: Heim Manuel; Johnson James; Boess Franziska; Bendik Igor; Weber Peter; Hunziker Willi; Fluhmann Beat
CORPORATE SOURCE: Roche Vitamins Ltd, Research and Development, Department of Human Nutrition and Health, 4070 Basel, Switzerland.
SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2002 May) 16 (7) 718-20.
Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020501
Last Updated on STN: 20030105
Entered Medline: 20020506

AB **Phytanic** acid, a metabolite of the chlorophyll molecule, is part of the human diet and is present in normal human serum at low micromolar concentrations. It was previously shown to be a ligand of the 9-cis-retinoic acid receptor and peroxisome proliferator-activated receptor (PPAR) a. PPAR agonists are widely used in the treatment of **type 2 diabetes**. Here, we report that **phytanic** acid is not only a transactivator of PPARa, but it also acts via PPARb and PPARg in CV-1 cells that have been cotransfected with the respective full-length receptor and an acyl-CoA oxidase-PPAR-responsive element-luciferase construct. We observed that, in contrast to other fatty acids, **phytanic** acid at physiological concentrations enhances uptake of 2-deoxy-D-glucose in rat primary hepatocytes. This result could be explained by the increase in mRNA expression of glucose transporters-1 and -2 and glucokinase, as determined by quantitative real-time reverse transcriptase-polymerase chain reaction. Compared with the PPARg-specific agonist ciglitazone, **phytanic** acid exerts only minor effects on the differentiation of C3H10T1/2 cells into mature adipocytes. These results clearly demonstrate that **phytanic** acid acts via different PPAR isoforms to modulate expression of genes involved in glucose metabolism, thus suggesting a potential role of **phytanic** acid in the management of insulin resistance.

L8 ANSWER 21 OF 30 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:315491 SCISEARCH
THE GENUINE ARTICLE: 537JV
TITLE: **Phytanic** acid, a natural peroxisome proliferator-activated receptor agonist, regulates glucose metabolism in rat primary hepatocytes
AUTHOR: Heim M; Johnson J; Boess F; Bendik I; Weber P; Hunziker W; Fluhmann B (Reprint)
CORPORATE SOURCE: Roche Vitamins Ltd, Dept Human Nutr & Hlth, Res & Dev, Bldg 93-8-56, CH-4070 Basel, Switzerland (Reprint); Roche Vitamins Ltd, Dept Human Nutr & Hlth, Res & Dev, CH-4070 Basel, Switzerland; F Hoffmann La Roche & Co Ltd, Pharma Res, CH-4070 Basel, Switzerland; Univ Freiburg, Inst Biol 2, D-79104 Freiburg, Germany
COUNTRY OF AUTHOR: Switzerland; Germany
SOURCE: FASEB JOURNAL, (MAR 2002) Vol. 16, No. 3, pp. U48-U64. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0892-6638.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Phytanic** acid, a metabolite of the chlorophyll molecule, is part of the human diet and is present in normal human serum at low micromolar concentrations. It was previously shown to be a ligand of the 9-cis-retinoic acid receptor and peroxisome proliferator-activated receptor (PPAR)alpha. PPAR agonists are widely used in the treatment of

type 2 diabetes. Here, we report that **phytanic** acid is not only a transactivator of PPARalpha, but it also acts via PPARbeta and PPARgamma in CV-1 cells that have been cotransfected with the respective full-length receptor and an acyl-CoA oxidase-PPAR-responsive element-luciferase construct. We observed that, in contrast to other fatty acids, **phytanic** acid at physiological concentrations enhances uptake of 2-deoxy-D-glucose in rat primary hepatocytes. This result could be explained by the increase in mRNA expression of glucose transporters-1 and -2 and glucokinase, as determined by quantitative real-time reverse transcriptase-polymerase chain reaction. Compared with the PPARgamma-specific agonist ciglitazone, **phytanic** acid exerts only minor effects on the differentiation of C3H10T1/2 cells into mature adipocytes. These results clearly demonstrate that **phytanic** acid acts via different PPAR isoforms to modulate expression of genes involved in glucose metabolism, thus suggesting a potential role of **phytanic** acid in the management of insulin resistance.

L8 ANSWER 22 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002164911 EMBASE
TITLE: The mode of action of thiazolidinediones.
AUTHOR: Hauner H.
CORPORATE SOURCE: H. Hauner, German Diabetes Research Institute, Heinrich-Heine University, Auf'm Hennekamp 65, D-40225 Dusseldorf, Germany. hauner@dfi.uni-duesseldorf.de
SOURCE: Diabetes/Metabolism Research and Reviews, (2002) 18/SUPPL. 2 (S10-S15).
Refs: 59
ISSN: 1520-7552 CODEN: DMRRFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The thiazolidinediones (TZDs) or 'glitazones' are a new class of oral antidiabetic drugs that improve metabolic control in patients with **type 2 diabetes** through the improvement of insulin sensitivity. TZDs exert their antidiabetic effects through a mechanism that involves activation of the gamma isoform of the peroxisome proliferator-activated receptor (PPARγ), a nuclear receptor. TZD-induced activation of PPARγ alters the transcription of several genes involved in glucose and lipid metabolism and energy balance, including those that code for lipoprotein lipase, fatty acid transporter protein, adipocyte fatty acid binding protein, fatty acyl-CoA synthase, malic enzyme, glucokinase and the GLUT4 glucose transporter. TZDs reduce insulin resistance in adipose tissue, muscle and the liver. However, PPARγ is predominantly expressed in adipose tissue. It is possible that the effect of TZDs on insulin resistance in muscle and liver is promoted via endocrine signalling from adipocytes. Potential signalling factors include free fatty acids (FFA) (well-known mediators of insulin resistance linked to obesity) or adipocyte-derived tumour necrosis

factor-α (TNF-α), which is overexpressed in obesity and insulin resistance. Although there are still many unknowns about the mechanism of action of TZDs in **type 2 diabetes**, it is clear that these agents have the potential to benefit the full 'insulin resistance syndrome' associated with the disease. Therefore, TZDs may also have potential benefits on the secondary complications of **type 2 diabetes**, such as cardiovascular disease. Copyright .COPYRGT. 2002 John Wiley & Sons, Ltd.

L8 ANSWER 23 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001263903 EMBASE
TITLE: PPARγ/RXR as a molecular target for **diabetes**.
AUTHOR: Lenhard J.M.
CORPORATE SOURCE: J.M. Lenhard, Department of Metabolic Diseases, GlaxoSmithKline Inc., 5 Moore Drive, Research Triangle Park, NC 27709, United States
SOURCE: Receptors and Channels, (2001) 7/4 (249-258).
Refs: 141
ISSN: 1060-6823 CODEN: RCHAE4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Type 2 diabetes** is associated with insulin resistance in peripheral tissues, such as muscle and fat. Novel therapies that improve insulin action include ligands that bind and activate the nuclear receptors peroxisome proliferator activating receptor γ (PPARγ) and retinoid X receptor (RXR). PPARγ/RXR form heterodimers that regulate transcription of genes involved in insulin action, adipocyte differentiation, lipid metabolism and inflammation. PPARγ activators include prostanoids, fatty acids, thiazolidinediones and N-(2-benzoylphenyl)tyrosine analogues. RXR ligands include naturally occurring retinoic acid and synthetic rexinoids. Selective ligands for these receptors improve metabolic abnormalities associated with **type 2 diabetes**, such as hyperglycemia, hyperlipidemia, insulin resistance and other cardiovascular risk factors. Although adipose tissue mediates some of the effects of PPARγ/RXR ligands, other tissues also regulate the effects of these receptors. The activity of the PPARγ/RXR heterodimer is influenced by posttranslational modifications, receptor turnover, polymorphisms, splice variants, coactivators and corepressors. This article reviews recent developments in research on these receptors, with particular emphasis on metabolic effects, ligand selectivity, structure and regulation of the PPARγ/RXR heterodimer.

L8 ANSWER 24 OF 30 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001373367 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11425290

TITLE: The chlorophyll metabolite **phytanic** acid is a natural rexinoid--potential for treatment and prevention of **diabetes**.
AUTHOR: McCarty M F
CORPORATE SOURCE: Pantox Laboratories, 4622 Santa Fe Street, San Diego, CA 92109, USA.
SOURCE: Medical hypotheses, (2001 Feb) 56 (2) 217-9.
Journal code: 7505668. ISSN: 0306-9877.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB Synthetic ligands of the retinoid X receptor (RXR) have shown antidiabetic activity in mice, apparently owing to the fact that they stimulate the transcriptional activity of PPAR-gamma/RXR heterodimers, much like thiazolidinedione drugs. The chlorophyll metabolite **phytanic** acid has been shown to be a natural ligand for RXR, active in concentrations near its physiological levels. It is thus reasonable to suspect that **phytanic** acid may have utility for treatment and prevention of human **type 2 diabetes**.
Phytanic acid may mimic or complement various effects of conjugated linoleic acids, which have been shown to activate PPAR-gamma/RXR and prevent rodent **diabetes**. Administration of hydrolyzed chlorophyll may represent the most cost-effective strategy for raising human tissue levels of **phytanic** acid.

L8 ANSWER 25 OF 30 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:753512 SCISEARCH
THE GENUINE ARTICLE: 472TJ
TITLE: The role of PPAR alpha in obesity
AUTHOR: Seedorf U (Reprint); Assmann G
CORPORATE SOURCE: Univ Munster, Clin Res Ctr, Inst Arteriosclerosis Res & Interdisciplinary, Dimagkstr 3, D-48149 Munster, Germany (Reprint); Univ Munster, Clin Res Ctr, Inst Arteriosclerosis Res & Interdisciplinary, D-48149 Munster, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: NUTRITION METABOLISM AND CARDIOVASCULAR DISEASES, (JUN 2001) Vol. 11, No. 3, pp. 189-194.
Publisher: MEDIKAL PRESS S R L, VIA LUIGI ZOJA, 30, 20153 MILAN, ITALY.
ISSN: 0939-4753.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Obesity is a rapidly increasing health problem in all developed countries. Overweight rarely occurs in isolation but as part of a complex pattern of metabolic abnormalities ("metabolic syndrome" or "syndrome X") consisting of hyperlipidemia, hypoalphalipoproteinemia, **type II diabetes** and atherosclerosis. The disorder is

considerably influenced by genetic, behavioural and nutritional factors. Recent data indicate that a group of closely related nuclear receptors, the peroxisome proliferator-activated receptors (PPARs), may, be involved in the metabolic changes ultimately leading to obesity. This review summarises the latest developments in the PPAR field, with particular emphasis being placed on the physiological function of PPAR alpha during various nutritional states, and the possible role of PPARa in obesity.

L8 ANSWER 26 OF 30 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1999352945 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10424146
TITLE: A case of motor and sensory polyneuropathy with retinitis pigmentosa and diffuse idiopathic skeletal hyperostosis.
AUTHOR: Osoegawa M; Araki E; Arakawa K; Okayama A; Yamada T; Ohnishi A; Kira J
CORPORATE SOURCE: Department of Neurology, Faculty of Medicine, Kyushu University.
SOURCE: Rinsho shinkeigaku. Clinical neurology, (1999 May) 39 (5) 542-5.
Journal code: 0417466. ISSN: 0009-918X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 20000303
Entered Medline: 19990924

AB We here report a 53-year-old man who presented with motor and sensory polyneuropathy, retinitis pigmentosa and diffuse idiopathic skeletal hyperostosis (DISH). He had a 15-year history of **diabetes** mellitus (DM). Visual impairment appeared at 17 years of age. Since age 47, he showed a slowly progressive sensory impairment and muscle weakness of the extremities. On neurological examination, retinitis pigmentosa and severe muscle atrophy, muscle weakness and sensory disturbance of all modalities in the distal portions of all four extremities were observed. Deep tendon reflexes were absent. A plain X-P showed diffuse ossification of the spinal and extraspinal ligaments. The motor nerve conduction velocities were severely reduced and no sensory nerve action potentials were evoked. The CSF examination revealed an increased protein level without pleocytosis. The sural nerve biopsy showed a marked onion bulb formation and a loss of the myelinated nerve fibers, which could not be solely explained by DM. As the **phytanic** acids levels, beta-lipoprotein, lactate and pyruvate in the sera were within the normal ranges, Refsum disease, Bassen-Kornzweig syndrome and mitochondrial diseases were unlikely in this patient. The presence of demyelinating and axonal polyneuropathy in this patient may have been caused by a common metabolic disturbance which produced both retinitis pigmentosa and DISH.

L8 ANSWER 27 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1993:321644 BIOSIS
DOCUMENT NUMBER: PREV199396029994
TITLE: Complementation analysis of patients with intact peroxisomes and impaired peroxisomal beta-oxidation.

AUTHOR(S): McGuinness, M. C. [Reprint author]; Moser, A. B. [Reprint author]; Poll-The, B. T.; Watkins, P. A. [Reprint author]
CORPORATE SOURCE: Kennedy Krieger Inst., Johns Hopkins Univ. Sch. Med., Baltimore, MD 21205, USA
SOURCE: Biochemical Medicine and Metabolic Biology, (1993) Vol. 49, No. 2, pp. 228-242.
CODEN: BMMBES. ISSN: 0885-4505.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jul 1993
Last Updated on STN: 31 Aug 1993

AB Complementation analysis, using peroxisomal beta-oxidation of very long chain fatty acids (VLCFA) as the criterion for complementation, is useful in the study of patients who are suspected of having a single enzyme defect in the peroxisomal beta-oxidation pathway. Laboratory findings for these patients include elevated plasma VLCFA and impaired VLCFA oxidation in fibroblasts. Some of these patients have slightly abnormal **phytanic** acid oxidation in fibroblasts. In addition, elevatd levels of bile acid intermediates have been reported in some cases. Plasmalogen synthesis, pipecolic acid levels, and subcellular distribution of catalase are normal. Using complementation analysis, we show that six patients, who were suspected of having a single enzyme defect in the peroxisomal beta-oxidation pathway, are deficient in peroxisomal bifunctional enzyme (enoyl-CoA hydratase (EC 4.2.1.17)/3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35)) activity. This group of six patients, deficient in bifunctional enzyme activity, may be subdivided into two complementation groups. It would appear that patients in each of these two groups are deficient in only one of the bifunctional enzyme activities.

L8 ANSWER 28 OF 30 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 92:329810 SCISEARCH
THE GENUINE ARTICLE: HV099
TITLE: ALPHA-OXIDATION OF FATTY-ACIDS IN FASTED OR **DIABETIC** RATS
AUTHOR: TAKAHASHI T (Reprint); TAKAHASHI H; TAKEDA H; SHICHIRI M
CORPORATE SOURCE: KUMAMOTO UNIV, SCH MED, DEPT METABOL MED, 1-1-1 HONJO, KUMAMOTO 860, JAPAN (Reprint); GINKYO COLL SCI, KUMAMOTO, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: DIABETES RESEARCH AND CLINICAL PRACTICE, (MAY 1992) Vol. 16, No. 2, pp. 103-108.
ISSN: 0168-8227.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Induction of alpha-oxidation, a possible gluconeogenic process, which should produce odd-chain fatty acids from even-chain fatty acids, was studied in rats fasted or made **diabetic** with streptozotocin. When a omega-phenylated even-chain fatty acid, phenylbutyric acid (1.2 mmol/kg), was administered to rats under these conditions, a significant increase in the urinary excretion of benzoic acid, the metabolic end-product of omega-phenylated odd-chain fatty acids, was observed in

fasted (3.54 +/- 0.46-mu-mol/day) and **diabetic** (6.73 +/- 2.10) rats (control, 0.58 +/- 0.43; P < 0.001). Phenylated longer chain fatty acids, phenylhexanoic and phenyldecanoic acid, did not produce significantly more benzoic acid than did phenylbutryic acid. Although the rate of alpha-oxidation was very low compared to that of beta-oxidation, these results suggested that alpha-oxidation of fatty acids was induced under fasting or **diabetic** conditions, and that alpha-oxidation might take place at the butyric acid stage.

L8 ANSWER 29 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 79210583 EMBASE
DOCUMENT NUMBER: 1979210583
TITLE: [Course of Refsum's disease treated by diet]. REFSUM KRANKHEIT UND IHR VERLAUF BEI DIATETISCHER BEHANDLUNG DURCH 2.5 JAHRE. KLINIK, BIOCHEMISCHE UND NEUROPATHOLOGISCHE DATEN.
AUTHOR: Lenz H.; Sluga E.; Bernheimer H.; et al.
CORPORATE SOURCE: Neurol. Inst., Univ. Wien, Austria
SOURCE: Nervenarzt, (1979) 50/1 (52-60).
CODEN: NERVAF
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
029 Clinical Biochemistry
022 Human Genetics
LANGUAGE: German
SUMMARY LANGUAGE: English

AB A report is given on the first case of Refsum disease observed in Austria. Treatment for it lasted 2 1/2 years. This was dietetic (Steinberg-/Stokke diet, plasmapheresis), which brought improvement of the clinical, biochemical and electrophysiological changes. Comparative bioptic examinations on the sural nerve made it possible to recognize and analyze widespread demyelinations and showed a regression of these and also considerable remyelinations and regenerations after almost 2 years' diet. The difficulties of dietetic therapy are examined in detail, and also its restorative effects on peripheral nerve tissue. There is a discussion on the relationship between the quantity of the biochemical changes and the manifestation of symptom-provoking changes with regard to the myelin.

L8 ANSWER 30 OF 30 JAPIO (C) 2005 JPO on STN

ACCESSION NUMBER: 2002-104964 JAPIO
TITLE: USE OF **PHYTANIC** ACID FOR TREATING **DIABETES**
INVENTOR: FLUEHMANN BEAT; HEIM MANUEL; HUNZIKER WILLI; WEBER PETER
PATENT ASSIGNEE(S): ROCHE VITAMINS AG
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 2002104964	A	20020410	Heisei	A61K031-20

APPLICATION INFORMATION
STN FORMAT: JP 2001-233070 20010801

ORIGINAL: JP2001233070 Heisei
PRIORITY APPLN. INFO.: EP 2000-116848 20000804
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2002

AN 2002-104964 JAPIO
AB PROBLEM TO BE SOLVED: To provide a method for preparing a product for the treatment and/or prevention of **non-insulin dependent diabetes** mellitus and related diseases such as syndrome X, hyperlipidaemia, hypertension, hyperinsulinaemia, hyperchloesterinaemia, hypertriglycerinaemia, especially impaired glucose tolerance and related obesity.
SOLUTION: **Phytanic** acid or its derivative, together with a pharmaceutically acceptable additive and/or adjuvant, is formulated into a pharmaceutical preparation.

(FILE 'MEDLINE' ENTERED AT 09:26:28 ON 18 FEB 2005)
L9 33267 SEA FILE=MEDLINE ABB=ON PLU=ON "DIABETES MELLITUS, TYPE 2"/CT
L10 296 SEA FILE=MEDLINE ABB=ON PLU=ON "PHYTANIC ACID"/CT
L11 1 SEA FILE=MEDLINE ABB=ON PLU=ON L9 AND L10

L11 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 2001373367 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11425290
TITLE: The chlorophyll metabolite phytanic acid is a natural rexinoid--potential for treatment and prevention of diabetes.
AUTHOR: McCarty M F
CORPORATE SOURCE: Pantox Laboratories, 4622 Santa Fe Street, San Diego, CA 92109, USA.
SOURCE: Medical hypotheses, (2001 Feb) 56 (2) 217-9.
Journal code: 7505668. ISSN: 0306-9877.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

ED Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802
AB Synthetic ligands of the retinoid X receptor (RXR) have shown antidiabetic activity in mice, apparently owing to the fact that they stimulate the transcriptional activity of PPAR-gamma/RXR heterodimers, much like thiazolidinedione drugs. The chlorophyll metabolite phytanic acid has been shown to be a natural ligand for RXR, active in concentrations near its physiological levels. It is thus reasonable to suspect that phytanic acid may have utility for treatment and prevention of human type 2 diabetes. Phytanic acid may mimic or complement various effects of conjugated linoleic acids, which have been shown to activate PPAR-gamma/RXR and prevent rodent diabetes. Administration of hydrolyzed chlorophyll may represent the most cost-effective strategy for raising human tissue levels of phytanic acid.

FILE 'HOME' ENTERED AT 09:27:15 ON 18 FEB 2005

Searcher : Shears 571-272-2528